IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BAYER HEALTHCARE AG, ALCON, INC. and ALCON RESEARCH, LTD. Plaintiffs, v. TEVA PHARMACEUTICALS USA, INC. Defendant.	)	Civil Action No. 06-234 (SLR) **PUBLIC VERSION OF SEALED DOCUMENT D.I. 115**

DEFENDANT TEVA PHARMACEUTICALS USA, INC.'S
POST-TRIAL REPLY BRIEF
ON THE INVALIDITY OF U.S. PATENT NO. 6,716,830

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I. Introduction

Alcon mischaracterizes various of Teva's proofs in hopes that the Court will ignore the contemporaneous record, a record which compels the conclusion that the '830 patent is invalid. Even where Alcon tries to address Teva's proofs, Alcon misstates the law, the facts, or both. Alcon's revisionist approaches to the prior art and the contemporaneous actions and experiences of Alcon and its inventors are akin to Alcon's attempts, in its briefs on infringement, to re-draft the '830 patent. Alcon's arguments are contrary to the facts and the law, and should be rejected. Claim 1 of the '830 patent is invalid.

II. Dr. Mitra's Testimony Should Be Excluded

A prime example of Alcon's mischaracterization (AAB,[1] pp. 40–42) is of Teva's motion to exclude Dr. Mitra's testimony and certain exhibits. Alcon treats Teva's motion *as if* it were based on merely a lost "opportunity to [re-]depose Dr. Mitra" (AAB, p. 40). This is not the issue: Teva seeks redress for Alcon's violation of Fed. R. Civ. P. 26(e), a violation which Alcon has not denied. Alcon's actions plainly prejudiced Teva, which was deprived of *notice* that Mitra's opinions *had changed*, as the trial transcript plainly illustrates (TOB[2], pp. 2–4).

Teva's motion also rests on Fed. R. Evid. 702, as Dr. Mitra has shown himself to be unreliable. Dr. Mitra's lack of candor is similar to his behavior before a sister Court, which was "troubled" by his "potentially misleading" testimony, perhaps not coincidentally, also concerning the impact of the "vehicle" on a formulation (*Roche Palo Alto LLC v. Apotex, Inc.*, 526 F. Supp. 2d 985, 993 n.2 (N.D. Cal. 2007), *aff'd*, No. 2008-1021, 2008 WL 2669287 (Fed. Cir. July 9, 2008)). While the court in that case did not address Dr. Mitra's apparent deceit, here, his change of position on a similar issue without proper notice to Teva should not be brushed aside.

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[1] "AAB" (Alcon's Answering Brief) refers to Plaintiff's Post-Trial Brief on Validity (D.I. 112).

[2] "TOB" refers to Teva's opening brief on the invalidity of the '830 patent (D.I. 107).

III. Claim 1 Of The '830 Patent Is Invalid In Light Of The Prior Art

A. The '942 Patent Anticipates Claim 1 Of The '830 Patent

Clear and convincing evidence proves that claim 1 is anticipated by Bayer's '942 patent. Tr. 186:17–193:5. Alcon (AAB, pp. 42–45) asserts that *Atofina v. Great Lakes Chem. Corp.*, 441 F.3d 991 (Fed. Cir. 2006), shows that the concentration range in claim 1 is not disclosed in the '942 patent, but *Atofina* is distinguishable for at least two reasons:

- The '942 patent inherently discloses a range of 0.1–0.5 wt. %: i.e., the difference between its two expressly disclosed, equally preferred, ranges. The inherent range falls entirely within[3] the claimed range of 0.1–1 wt. %, unlike the ranges at issue in *Atofina*, 441 F.3d at 999.
- Also unlike *Atofina*, the record evinces that a person of ordinary skill in the art (the proper standard (*see Finisar Corp. v. DirecTV Group, Inc.*, 523 F.3d 1323, 1336 (Fed. Cir. 2008)) would recognize the concentrations under 1 wt. % disclosed by the '942 patent to be useful for ophthalmic formulations.[4] Tr. 191:1–192:14. The '942 patent discloses the '830 patent's claimed range for ophthalmic use, and so anticipates claim 1.

Alcon's (AAB, pp. 45–48) argument that the '942 patent cannot anticipate claim 1 due to the breadth of its disclosure is contrary to Alcon's own reliance (in part) on one of the unnamed "billions" of compounds of that same broad disclosure to rescue its claim construction (AAB, p. 45, D.I. 111, p.4). If Alcon can credit the '942 patent with disclosing "moxifloxacin," reason

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[3] Alcon misleadingly implies (AAB, pp. 43–44) that the entire range (.1–1 wt. %) must be disclosed in the '942 patent for there to be anticipation. Rather, the disclosure of any point within the range is anticipatory. *See Titanium Metals Corp. of Am. v. Banner,* 778 F.2d 775, 781 (Fed. Cir. 1985); *Atlas Powder Co. v. IRECO, Inc.,* 190 F.3d 1342, 1346 (Fed. Cir. 1999).

[4] Far from being an "effort to combine the '942 patent with other prior art" (AAB, p. 43), Dr. Allen's reference to the Ciloxan® and Ocuflox® formulations merely "confirm[s] the contents of the allegedly anticipating reference," an approach that the Federal Circuit has endorsed. *Teleflex, Inc. v. Ficosa N.A. Corp.*, 299 F.3d 1313, 1335 (Fed. Cir. 2002); *accord In re Baxter Travenol Labs.*, 952 F.2d 388, 390 (Fed. Cir. 1991).

compels also recognizing the '942 patent's disclosure of formulating it for ophthalmic use.[5] Alcon provides no basis for asking the Court to selectively ignore portions of the '942 patent's disclosure; in fact, Alcon's approach is inconsistent with the law of anticipation. *See Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1376 (Fed. Cir. 2005) (rejecting an argument that a disclosure "cannot anticipate because it appears without special emphasis in a longer list"). Alcon's reference to *Finisar,* 523 F.3d 1323, also is misplaced because that case involved claims specifying process steps in a particular order. *Id.* at 1335. In contrast,[6] '830 claim 1 does not specify any particular order of its elements.[7] In the end, Alcon's focus on the many embodiments disclosed in the '942 patent ignores the fact that '830 claim 1 is among these alternative embodiments—the quintessence of anticipation.

B. Claim 1 Is Invalid As Obvious

1. Teva's *Prima Facie* Showing Of Obviousness Is Overwhelming

If the Court decides that *Atofina* compels a finding that '830 claim 1 is not anticipated, then '830 claim 1 is *presumed* to be obvious because the claimed range is within that disclosed by the '942 patent (which also discloses the other elements of claim 1). *See Iron Grip Barbell*

[5] Alcon's argument ignores the fact that the '942 patent discloses ophthalmic compositions with the same breadth as the '830 patent claims ophthalmic compositions. *See, e.g.,* PTX 3, col. 54, ll. 65–67 ("pharmaceutically acceptable excipients are to be understood as solid, semi-solid or liquid diluents, fillers and formulation auxiliaries *of all types*." (emphasis added)); *see also* PTX 3, col. 55, ll. 1–5, col. 54, ll. 47–52.

[6] Alcon misstates *Finisar's* ruling, which did not hold "the correlation of disparate disclosures from a reference to the claim elements insufficient to prove anticipation" (AAB, p. 48). Rather, *Finisar* recognized that such disparate disclosures of a reference should be read in concert when, as here, they concern the same subject matter, or where, as here, the author indicates a linkage. 523 F.3d at 1338. Thus, the '942 patent's repeated internal references to the "compounds according to the invention" within its disclosure of treatments and formulations, which include ophthalmic formulations and the concentration range (e.g., columns 53–56), indicate that this disclosure is to be read in concert with its disclosed and claimed compounds, e.g., "moxifloxacin" (according to Alcon's requested claim construction).

[7] Alcon also fails to argue how the '942 patent does not disclose the limitations arranged as in '830 claim 1. (AAB, pp. 47–48).

Co. v. USA Sports, Inc., 392 F.3d 1317, 1322 (Fed. Cir. 2004). In this case, the presumption is not rebutted, as the prior art did not teach away from the 0.1-1% range nor is there evidence that this range is associated with any unexpected results. *See id.* To the contrary, a person of ordinary skill would have *expected* concentrations under 1 wt. % to be particularly applicable to ophthalmic formulations (Tr. 191:1–192:4; DTX 144, Tr. 194:1–18; DTX 159, Tr. 220:10–221:8). Accordingly, the only possible difference (if any) between '830 claim 1 and the '942 patent is merely the product of routine experimentation, which is not patentable. *See, e.g., In re Aller*, 220 F.2d 454, 456 (C.C.P.A. 1955) ("[I]t is not inventive to discover the optimum or workable ranges by routine experimentation").

The prior art fully suggested the claimed invention. Dr. Stroman admitted—and none of Alcon's experts disputed—that moxifloxacin HCl was known to be active against bacteria associated with ocular infections (Tr. 660:16–661:16). Thus, there was ample motivation to formulate moxifloxacin HCl for topical ophthalmic use. Clear and convincing evidence proves:

- Moxifloxacin HCl was proven to have activity against *Staphylococcus aureus* (hereinafter "*SA*") and *Pseudomonas aeruginosa* (hereinafter "*PA*"), both of which cause ophthalmic infections (TOB, p. 18; DTX 4017, Tr. 477:18–479:6; PTX 1124, Tr. 479:19–481:5, Tr. 495:2–13, Tr. 660:16–661:16);
- Moxifloxacin HCl's activity against both *SA* and *PA* was proven to be better than that of ofloxacin, which was recognized as one of the "standards of care" for ophthalmic infections (TOB, p. 18; DTX 4017, Tr. 477:18–479:6, 459:8–14);
- Moxifloxacin HCl was not known to exhibit unacceptable toxicity. *Contra*, prior art literature suggested that moxifloxacin HCl was recognized as being well tolerated in humans (TOB, pp. 19–20; DTX 195, p. 1399; Tr. 528:2–529:20, 225:19–226:21; PTX 1098);

- Moxifloxacin HCl was proven to generate less bacterial resistance than ciprofloxacin (the other state of the art treatment for ophthalmic infections), and was even known to be active against *SA* strains that were resistant to other fluoroquinolones (TOB, pp. 18–19; PTX 1124, PTX 1125, Tr. 520:24–522:25, 1045:23–1047:2, 525:21–526:13, 1113:8–17, 459:8–22); and
- It was expected that moxifloxacin HCl would penetrate the ocular tissues to some degree, and better than "standard-of-care" ofloxacin (TOB, pp. 20–21; Tr. 786:21–787:18).

The prior art clearly shows, and Alcon does not dispute, that the person of ordinary skill (under either Teva's or Alcon's definitions) would have expected in September 1998 that topical ophthalmic compositions containing moxifloxacin HCl in a concentration of 0.1-1 wt. % would be useful in treating, *at the very least*, *some* ophthalmic infections, including conjunctivitis, which the '830 patent contemplates. PTX 5, col. 2, ll. 23-25. *See KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727, 1742 (2007) ("[A]ny need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.") Even Dr. Alfonso's professed skepticism extended only to whether topical ophthalmic moxifloxacin HCl would be "developed," not whether it would act as an antibiotic in ophthalmic compositions. Tr. 490:18–492:2, 494:13–495:13, 488:19–489:21. This is consistent with Dr. Allen's testimony. Tr. 223:5–12, 224:11–24.

It is also unrebutted that "on a purely mechanical level, a skilled artisan would have a reasonable expectation of success of manufacturing a [moxifloxacin HCl ophthalmic] formulation within the limitations of the asserted patent claim[]." *Alza Corp. v. Mylan Labs., Inc.*, 388 F. Supp. 2d 717, 739 (N.D.W. Va. 2005), *aff'd,* 464 F.3d 1286 (Fed. Cir. 2006). This, in view of the reasonable expectation that moxifloxacin HCl would be useful to treat at least some ophthalmic infections in a concentration range and formulation similar (if not identical) to

that of other marketed fluoroquinoloes, proves obviousness.[8] The facts clearly and convincingly show that the "predictable use of prior art elements according to their established functions" reflected in '830 claim 1 would have been obvious to a person of ordinary skill. *KSR*, 127 S. Ct. at 1740 (2007); *Daiichi Sankyo Co. v. Apotex, Inc.*, 501 F.3d 1254, 1258 (Fed. Cir. 2007).

2. Alcon's Efforts To Rebut Teva's *Prima Facie* Showing Fail

a. Alcon's "Definition" Of A Person Of Ordinary Skill In The Art Is Unhelpful, And It Should Be Rejected

Teva does not propose to strike the phrase "and/or" from the English language. However, Alcon's use of it here is simply a mechanism through which it seeks to muddle the record with the testimony of experts with vastly and admittedly inconsistent expertise (TOB, pp. 29-30). Dr. Zhanel is not competent to testify as to matters within the purview of an M.D. (Tr. 987:25-988:6), nor does Dr. Alfonso have a Ph.D in microbiology (Tr. 446:1).[9]

b. Alcon's Assertion For The "Requirements" For New Ophthalmic Compositions Are Undercut By Its Own Experts And Actions

Having no response to Teva's *prima facie* case of obviousness, Alcon overhypes matters of no practical significance to the obviousness inquiry: Vigamox®'s activity against *PA* (relative to that of Ciloxan®) and Vigamox®'s ability to treat "deep ocular infections" (AAB, p.13–24). Alcon's contentions are litigation-inspired and inconsistent with Alcon's own experience in the real world: undeniably, Alcon sought and obtained FDA approval for Vigamox® only for the treatment of conjunctivitis and not deep ocular infections (See DTX 137; Tr. 541:17–543:11) and

[8] The Supreme Court's recognition in *KSR*, 127 S. Ct. at 1740, that "if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill" has particular applicability in this case.

[9] Unlike Alcon's proposal here, the cases cited by Alcon (AAB, p. 11, fn. 2) use "and/or" to allow for alternative academic degrees or professional experience (e.g., M.D. vs. Ph.D.; designer vs. manufacturer) within common fields of expertise (e.g., bisphosphonates, ostoporosis, pharmacology, biomedical devices) but not to conflate different fields disclaimed by experts.

not for the treatment of *PA* (Tr. 543:1–8). All of this reveals that moxifloxacin HCl's impact on deep ocular infections and activity against *PA* were not prerequisites to Alcon, the FDA, or even physicians for using moxifloxacin HCl as a topical ophthalmic pharmaceutical.

Faced with the inconsistency between its litigation contentions and its real-world experience, Alcon (AAB, p. 14, fn. 4) attempts to dismiss the fact that Vigamox®'s approved indication is for the treatment of non-*PA* conjunctivitis.[10] This completely ignores the importance Alcon (and its inventors) placed on the treatment of non-*PA*, non-deep ocular infections in September 1998, as shown by:

- Dr. Abshire's (an Alcon employee/inventor) reference to Dr. Cagle's (another Alcon employee/inventor) desire for "a once-a-day dosing regimen for conjunctivitis" (DTX 64);
- Dr. Abshire's recognition that moxifloxacin HCl's activity against *PA* relative to that of ciprofloxacin would not have clinical effect (DTX 64); and
- Alcon's inclusion of conjunctivitis in the '830 patent as the first condition in the list of conditions contemplated being treated with "moxifloxacin" (PTX 5, col. 2, ll. 23–29).

In fact, no record within Alcon contemporaneous with filing its patent application signaled any special importance of using moxifloxacin HCl to treat *PA* or of treating only deep eye infections. Thus Alcon's real-world experience with moxifloxacin HCl conflicts with the issues Alcon concocted for purposes of this litigation.

Alcon's expert's testimony on this issue is similarly suspect: Dr. Alfonso dismissed the FDA's approval for conjunctivitis (Tr. 543:1-24). However, he conceded that Vigamox® is an

[10] Alcon's protestations regarding the "exigencies of the regulatory process" (AAB, p. 14 fn. 4) notwithstanding, it would, of course, be illegal for Alcon to "introduce [Vigamox®] into interstate commerce with an intent that it be used for an off-label purpose." *Washington Legal Found. v. Henney*, 202 F.3d 331, 332–33 (D.C. Cir. 2000) (citing 21 U.S.C. § 331(d)); *see also United States v. Caputo*, 288 F. Supp. 2d 912, 921 (N.D. Ill. 2003).

acceptable "topical ophthalmic pharmaceutical composition" (Tr. 543:1–11) even absent its approval for treatment of deep tissue infections or for treating *PA*. Dr. Zhanel's speculation that "[t]here was no need for a new drug for conjunctivitis" (Tr. 1019:1–1020:2) is inconsistent with (a) Alcon's decision to market Vigamox® only for conjunctivitis[11] (b) the very language in the '830 patent, by which Alcon and its inventors revealed there was a need for new treatments for conjunctivitis (PTX 5, col. 2, ll. 23–29), and (c) contemporaneous internal Alcon communications regarding the usefulness of moxifloxacin HCl (DTX 64).

Alcon's attempt here to walk away from its history is plainly rooted in the "exigencies of the [litigation] process." *See* AAB, p. 14 fn. 4. Superior ability to treat *PA* simply was not a requisite in 1998, nor was treatment of "deep ocular infections." The absence of both of these posed no barrier to the FDA's approval of Vigamox®. Alcon's focus on issues that simply were not major concerns in September 1998 does not rebut Teva's proof of obviousness.

c. Alcon's Selection Argument Is Misplaced

Alcon's assertion that the invention of the '830 patent is somehow the "selection" of moxifloxacin is undermined by the very case law it cites (AAB, pp. 4–5, 27–28). A close reading of these cases reveals that each involved the question of whether a chemical *compound*, as opposed to a formulation (as in the '830 patent), would have been obvious. That issue is manifestly different from the question in this case: whether it would have been obvious to formulate a known fluoroquinolone with known antibacterial properties similarly if not identically to known (and successful) formulations of other known flouroquinolones.

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[11] Dr. Zhanel's concession that Alcon (which clearly regarded treatment of conjunctivitis as important) had vastly more experience with eye-care than himself (Tr. 1063:7–18) is significant. Dr. Zhanel's speculation concerning what was needed in the eye-care market is mere puffery and should be accorded very little, if any, weight. In any event, Dr. Zhanel ultimately conceded that, despite his interpretation of the "problem" addressed by the '830 patent, compositions for the treatment of conjunctivitis are within the scope of claim 1. Tr. 1018:7–1022:7.

The '942 patent "selected" moxifloxacin and disclosed its ophthalmic formulation and use. It is the '942 patent which might raise the "lead compound" issue as in the cases cited by Alcon, not the '830 patent.[12] Thus Alcon's arguments as to the "selection" of moxifloxacin, and to "teaching away" are misplaced. Alcon's "selection" argument also ignores *Daiichi*, 501 F.3d 1254, in which, as here, the use of a known fluoroquinolone with known antibacterial properties similarly to another known fluoroquinolone antibiotic was held to have been obvious.

d. Dr. Allen Provided Helpful Testimony

Dr. Allen's explanation of how a person of ordinary skill in the art would view prior art is in line with how the real world works. Alcon's accusation that Dr. Allen impermissibly relied on hindsight (AAB, pp. 25, 29–32, 47) is not in accord with the record *as a whole*; it ignores Dr. Allen's extensive treatment of the prior art from the perspective of the person of ordinary skill. *See MuniAuction, Inc. v. Thomson Corp.*, --- F.3d ----, No. 2007-1485, 2008 WL 2717689 at *6 (Fed. Cir. July 14, 2008). Dr. Allen's recognition that the inventors acted[13] as would a person of ordinary skill is not "hindsight." It merely illustrates that the inventors did nothing new and had no more knowledge or insight about moxifloxacin HCl than a person of ordinary skill.

Alcon (AAB, p. 5) also complains that Dr. Allen did not address the ultimate legal issue of obviousness. Yet it is plain from Dr. Allen's testimony that he regarded the substitution of moxifloxacin HCl from the '942 patent for other fluoroquinolone compounds in commercial topical ophthalmic formulations to have been not only obvious, but "foolish not to do it." (e.g., Tr. 200:8-16; 245:2-8). In any event, Alcon's fluster over the ultimate question is meaningless to

[12] Alcon (AAB, p. 28, fn. 6) implicitly acknowledges this by citing *Bayer AG v. Dr. Reddy's Labs., Ltd.*, 518 F. Supp. 2d 617 (D. Del. 2007), in which the '942 patent was at issue.

[13] Contrary to Alcon's accusation (AAB, p. 29), Teva does not seek to use the actions of the inventors to "negative" the '830 patent. Moreover, the inventors' derivation of knowledge of BAY 12-8039 and of other topical ophthalmic formulations from Bayer and others– which is 102(f) prior art (as well as 102(a) and (b) prior art) – is a permissible area of inquiry for obviousness. *See OddzOn Prods., Inc. v. Just Toys, Inc.*, 122 F.3d 1393, 1403 (Fed.Cir.1997).

the analysis. *Nutrition 21 v. United States*, 930 F.2d 867, 871 n.2 (Fed. Cir. 1991) (noting that an expert's opinion on an ultimate legal conclusion of obviousness is neither required nor evidence).

e. Secondary Considerations Do Not Rebut Obviousness

Alcon's evidence of unexpected properties is based on a single, optimized formulation: Vigamox®, an ophthalmic solution having 0.5% moxifloxacin HCl in a very specific vehicle (AAB, pp. 34–35). Alcon does not rely on the properties of any ointment, gel, suspension, solid, semisolid, or any other type of composition within '830 claim 1's scope. PTX 5, col. 5, ll. 47-51; Tr. 665:18–666:1, 664:14–665:6. Alcon has made no effort to address the properties of any "salts or hydrates" of moxifloxacin other than the HCl salt (i.e., BAY 12-8039). Alcon does not even assert that any composition other than Vigamox® has been shown to meet the overly-restrictive "long-felt need" Alcon purports (AAB, p. 34). Accordingly, any secondary considerations here lack the required nexus with claim 1 of the '830 patent to rebut its obviousness. *See MuniAuction,* 2008 WL 2717689 at *7.

Alcon's assertion (AAB, p. 39) that the same ocular penetration would be seen regardless of dosage form runs directly contrary to Dr. Mitra's admission that inactive excipients *do*, in fact, materially effect ocular penetration (Tr. 757:1–760:10).[14]

Moreover, Alcon's Vigamox® is an optimized solution, yet *none* of the inventors was involved in the optimization of Vigamox® (Tr. 674:4–13). Thus, any commercial success or

[14] Even if, despite Teva's motion, the Court accepts Dr. Mitra's testimony, his statements that moxifloxacin penetrates occular tissues is not probative of the obviousness of claim 1. He conceded that a person of ordinary skill *would have expected moxifloxacin* to penetrate the ocular tissues *to some degree*. Tr. 786:21–787:18. Any difference in the ocular penetration of moxifloxacin HCl and this expectation, thus, is merely one of degree, and is "not truly [an] unexpected result[]." *In re Merck & Co.*, 800 F.2d 1091, 1099 (Fed. Cir. 1986). Second, Dr. Mitra admitted that the model on which he relied does not allow "extrapolat[ion] this time with what happens in the eye when you put a drop. So these *are two different things*." Tr. 807:2–13 (emphasis added). His testimony, therefore, has no bearing on any "pharmaceutical" formulation containing moxifloxacin.

properties of Vigamox® are legally irrelevant because such are attributable to improvements or modifications (i.e., optimization[15]) made by others and not contemplated by the inventors. *MuniAuction*, 2008 WL 2717689 at *7 ("secondary considerations may presumptively be attributed to the patented invention only where the marketed product embodies the claimed features, *and is coextensive with them*" (citations omitted, emphasis added)); *Pfizer Inc. v. Teva Pharms. USA, Inc.*, 460 F. Supp. 2d 659, 666–67 (D.N.J. 2006) (secondary considerations due to features not contemplated at the time of invention are not probative of nonobviousness).

In essence, Alcon contends that if Vigamox® were itself somehow not obvious, then claim 1 of the '830 patent also is not obvious. This is contrary to the law. *See, e.g., MuniAuction*, 2008 WL 2717689 at *7 n.4 (noting that even if patentable subject matter may be included in breadth of claim, "claims which are broad enough to read on obvious subject matter are unpatentable." (citation omitted)). The record contains overwhelming evidence that many compositions within the scope of claim 1—such as, at least, the examples of the '830 patent, which merely substitute moxifloxacin for other fluoroquinolones in otherwise known formulations (TOB, pp. 15–17, 32–33)—would have been obvious.

Dr. Zhanel's exhaustive lecture on fluoroquinolone toxicity (Tr. 907:8–949:13) is likewise uninformative because none of the cautionary tales he told involved moxifloxacin. The vague "skepticism"[16] alluded to by Dr. Alfonso (AAB, p. 34) is entirely speculative, as he could not identify when, where, or, other than in the most general terms, who expressed this alleged "skepticism." Tr. 415:2–416:10; 487:14–488:14. Even if moxifloxacin HCl had been known to be systemically toxic, Alcon may well have pursued it for ophthalmic use notwithstanding, as

[15] Alcon also admits (AAB, p. 7) that "optimization is nowhere reflected in the '830 patent."

[16] It is notable that Dr. Alfonso admitted that his "skepticism" did not extend to whether topical ophthalmic moxifloxacin was an antibacterial agent. Tr. 488:19–489:21.

Alcon and others pursued many of the same fluoroquinolones that Dr. Zhanel identified as being systemically toxic. DTX 238, 229, 232, 227, 233, 230, 234; Tr. 1066:4–1069:2, 1069:21–1073:9, 1073:17–1076:3, 1076:12–1078:14, 1078:21–1081:1, 1081:2–1083:20, 1083:21–1086:13; TOB, pp. 8–10.

IV. The '830 Patent Fails To Comply With 35 U.S.C. § 112, First Paragraph

A. The '830 Patent Does Not Disclose The Best Mode

It remains undisputed that Dr. Stroman knew of only one mode of practicing his invention, the use of BAY 12-8039 (i.e., Bayer's trade name for moxifloxacin HCl (an S,S enantiomer)), and that this best—and only—mode is not disclosed in the '830 patent. This violates Section 112, ¶1 (TOB, pp. 40-43), and Alcon's arguments do not show otherwise:

- Alcon's contention (AAB, pp. 48–51) that Dr. Stroman had no preference for one active ingredient over another is simply wrong: he specifically requested Bayer's "BAY 12-8039" using Bayer's tradename. PTX 1065. Whether he knew the structure of BAY 12-8039 is immaterial. *U.S. Gypsum Co. v. Nat'l Gypsum Co.*, 74 F.3d 1209, 1214 (Fed. Cir. 1996) (disclosure of supplier/trade name information was required to satisfy best mode when that was the only information known to the inventor).
- Alcon's assertion (AAB, pp. 52–53) that the failure to disclose the best mode can be remedied through the knowledge of a person of ordinary skill is contrary to precedent. *Bayer AG v. Schein Pharms., Inc.*, 301 F.3d 1306, 1314 (Fed. Cir. 2002) (failure to disclose best mode cannot be remedied "by mute reference to the knowledge of one of skill in the art.")
- Alcon's contention (AAB, pp. 50–52) that the use of moxifloxacin betaine instead of the HCl makes no difference is contradicted by Drs. Taylor (Tr. 95:6–13, 143:11–22) and Alfonso (Tr. 461:8–18). Alcon's (AAB, p 51, fn.25) acknowledgement that some "buffering" (to

adjust pH)[17] would be required if moxifloxacin betaine were used instead of HCl further confirms the material effect that the HCl salt has in making the formulation. *See Bayer*, 301 F.3d at 1321; *Cardiac Pacemakers, Inc. v. St. Jude Medical, Inc.*, 381 F.3d 1371, 1378 (Fed. Cir. 2004) ("best mode violation requires that the inventor knew of and concealed a better mode than was disclosed for ***making*** *and using* the claimed invention" (emphasis added)).

- Ms. Alford's 2007 experiment[18] showing that moxifloxacin betaine can be dissolved is irrelevant, as such information was not known to the inventors in 1998, at the time of the patent's filing. *Engel Indus., Inc. v. Lockformer Co.*, 96 F.3d 1398, 1407 (Fed. Cir. 1996).
- The material differences between moxifloxacin HCl and betaine are further confirmed by the testimony provided by Dr. Petersen, an inventor of moxifloxacin (PTX 3), to this Court in a previous case (see TOB, p. 43).[19]

B. Alcon's Persons Of Ordinary Skill Cannot Practice The Full Scope Of Claim 1 Without Undue Experimentation

Alcon (AAB, p. 53) would now like to "agree" that the '830 patent somehow enables its persons of ordinary skill to make the invention without undue experimentation, but that is simply

[17] As Dr. Alfonso testified, the pH of an ophthalmic solution can materially affect the properties of the solution. Tr. 461:8–18.

[18] Ms. Alford did not make the full scope of claim 1 of the '830 patent, as she only made solutions, and not any gels, solids, suspensions, or any other dosage form; thus, her testimony cannot rescue the claim. *See Sitrick v. Dreamworks, LLC*, 516 F.3d 993, 1000 (Fed. Cir. 2008). Her work is further irrelevant, since the solutions she made do not have the characteristics necessary to be a "pharmaceutical" (Tr. 690:4–25) and so are not in accordance with claim 1.

[19] Despite Alcon's protestations (AAB, p. 51), Dr. Petersen's testimony is not "plainly" hearsay. *See, e.g.,* Fed. R. Evid. 804(b)(1) (Bayer, from whom Alcon has licensed the '942 patent for moxifloxacin such that they are in a community of interest, elicited his testimony); Fed. R. Evid. 807 (there is no reason to doubt that Dr. Petersen's testimony was truthful; Alcon had notice in the Pretrial Order of the difference between moxifloxacin betaine and HCl). Even if it were hearsay, Dr. Petersen's testimony (statements of an inventor of moxifloxacin) is no different in kind than (and rebuts) the hearsay relied on by Alcon and its expert (AAB, p. 52, Tr. 1040:22-1041:4) in an attempt to mischaracterize Bayer's belief of moxifloxacin betaine and its salts as being "interchangeable;" thus the "state of mind" exception and/or Fed. R. Evid. 703 would apply.

not supported by the facts. Rather, such persons are not actually capable of making formulations throughout the scope of claim 1. *See* TOB, pp. 45–50. In response, Alcon (AAB, pp. 53–56) clings to the conclusory, unsupported testimony of Drs. Alfonso and Zhanel. This is exactly the type of evidence that the Courts have repeatedly rejected as unhelpful. *See, e.g., Daubert v. Merrell Dow Pharms., Inc.*, 113 S. Ct. 2786, 2795 (1993), *Calhoun v. Yamaha Motor Corp*, 350 F.3d 316, 322 (3rd Cir. 2003); *In re Paoli*, 35 F.3d 717, 742 (3rd Cir. 1994); *Izumi Prods. Co. v. Koninklijke Philips Elecs. N.V.*, 315 F. Supp. 2d 589, 602 (D. Del. 2004).

Both Drs. Alfonso (Tr. 446:12–15) and Zhanel (Tr. 1076:25–1078:3) disclaimed expertise in pharmaceutical compounding, which alone should compel the rejection of their opinions on this issue. *Betterbox Commc'ns. Ltd. v. BB Techs., Inc.*, 300 F.3d 325, 335 (3rd Cir. 2002) (expert's lack of testing and admission that "I'm not an expert" on relevant question compelled rejection of expert's opinion). Dr. Alfonso also admitted that he had not made *any* of the exemplary formulations listed in the '830 patent. Tr. 454:10–25. There is likewise no evidence that Dr. Zhanel ever made any formulations commensurate with the scope of claim 1. Despite Alcon's protestations otherwise, these conclusory, unsupported opinions do not rebut Teva's showing that Alcon's persons of skill in the art cannot make the full scope of claim 1 without far more guidance—in a field that Alcon's experts admit to be outside their areas of expertise—than is provided by the disclosure of the '830 patent (i.e., without undue experimentation). Accordingly, the '830 patent is invalid for lack of enablement.

C. Claim 1 Is Invalid For Overclaiming

Alcon incorrectly asserts (AAB, p. 56) that *Cooper Cameron Corp. v. Kvaerner Oilfield Prods., Inc.*, 291 F.3d 1317 (Fed. Cir. 2002), undermines *Gentry Gallery, Inc. v. Berkline Corp.*, 134 F.3d 1473 (Fed. Cir. 1998). In *Cooper*, though, the Federal Circuit merely restated the law: "[i]n *Gentry*, we applied and merely expounded upon the unremarkable proposition that a broad

claim is invalid when the entirety of the specification clearly indicates that the invention is of a much narrower scope." *Cooper*, 291 F.3d at 1323. This supports Teva's contention that the '830 patent is invalid because claim 1 (which does not require a preservative) is broader than the specification[20] (which states that a preservative is required, PTX 5, col. 5, l. 66–col. 6, l. 9). Moreover, the preservative is something separate from moxifloxacin. *In re Omeprazole*, Nos. 2007-1476, 2007-1477, 2007-1478, 2008 WL 2369864 at *5 (Fed. Cir. June 10, 2008) (specification's disclosure of talc in a general list of excipients, but not in list of "ARCs" (a specific type of excipient) indicates that talc is not an "ARC"). The '830 patent's statement that a preservative is "required" must be credited; [21] accordingly claim 1 is invalid for inadequate written description.

Furthermore, the overclaiming in claim 1 separately violates Section 112's enablement requirement (TOB, p. 45). *In re Mayhew*, 527 F.2d 1229, 1233 (C.C.P.A. 1976); *cf. MuniAuction*, 2008 WL 2717689 at *7 n.3 (lack of disclosure asserted to show nonobviousness instead suggested enablement violation). Alcon has declined even to address this issue.

V. Conclusion

For the reasons discussed in Teva's briefs, if the Court construes "moxifloxacin" as Alcon requests, then claim 1 is invalid under 35 U.S.C. § 103(a) as obvious and under 35 U.S.C. § 102(b) as anticipated. Regardless of the Court's claim construction, claim 1 of the '830 patent is invalid under 35 U.S.C. § 112.

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[20] Alcon's reliance on Example 3 ignores that it is plainly inconsistent with the patent specification's unambiguous statement that a preservative is required, and provides no indication that moxifloxacin can act as that preservative. *See Sinorgchem Co. v. ITC,* 511 F.3d 1132, 1138 (Fed. Cir. 2007).

[21] Alcon's (AAB p. 57) focus on the phrase "products are typically packaged in multidose form" is insufficient to support its argument. Claim 1 does not differentiate between multi-dose and single dose forms, nor does the specification state anything other than "[p]reservatives are thus required," and does not exempt any dosage form. PTX 5, col. 5, l. 66–col. 6, l. 1.

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